1st ref

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1626GMS

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 09	ACD predicted properties enhanced in REGISTRY/ZREGISTRY
NEWS	4	OCT 03	MATHDI removed from STN
NEWS	5	OCT 04	CA/CAplus-Canadian Intellectual Property Office (CIPO) added to core patent offices
NEWS	6	OCT 13	New CAS Information Use Policies Effective October 17, 2005
NEWS	7	OCT 17	STN(R) AnaVist(TM), Version 1.01, allows the export/download of CAplus documents for use in third-party analysis and visualization tools
NEWS	8	OCT 27	Free KWIC format extended in full-text databases
NEWS	9	OCT 27	DIOGENES content streamlined
NEWS	10	OCT 27	EPFULL enhanced with additional content
NEWS	11	NOV 14	CA/CAplus - Expanded coverage of German academic research

NEWS EXPRESS NOVEMBER 18 CURRENT VERSION FOR WINDOWS IS V8.01,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005.
V8.0 USERS CAN OBTAIN THE UPGRADE TO V8.01 AT
http://download.cas.org/express/v8.0-Discover/

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:21:31 ON 29 NOV 2005

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 10:21:46 ON 29 NOV 2005

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 28 NOV 2005 HIGHEST RN 868827-82-1
DICTIONARY FILE UPDATES: 28 NOV 2005 HIGHEST RN 868827-82-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

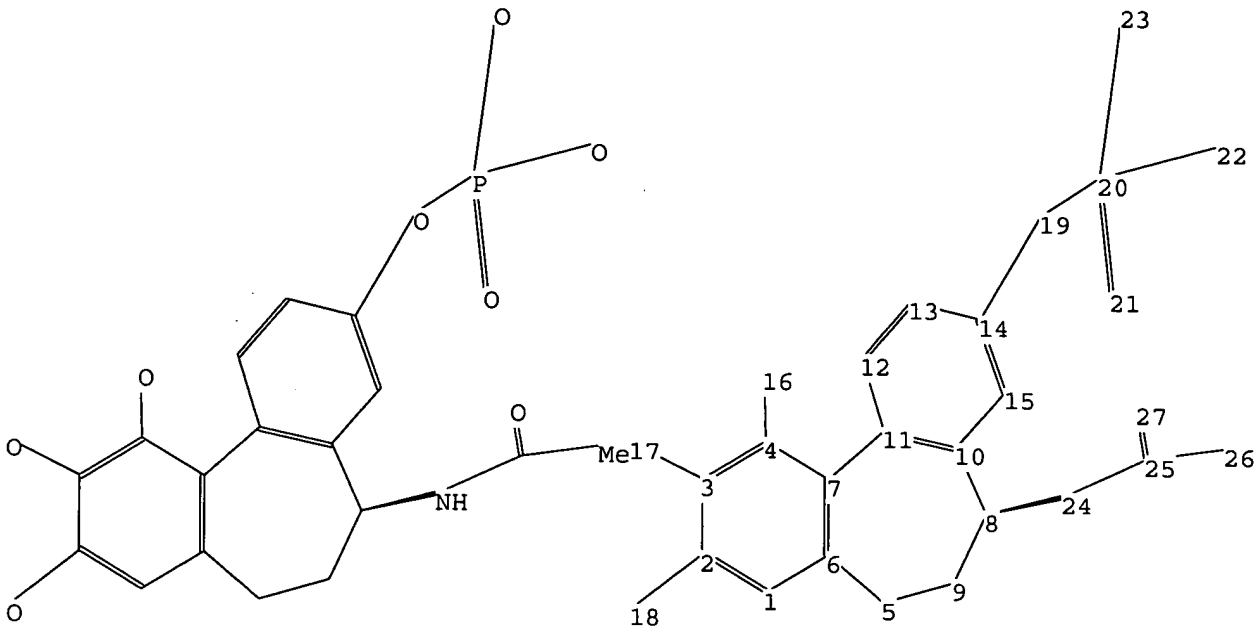
```
**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005. A new display format, IDERL, is now      *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************
```

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10731842.str



chain nodes :
16 17 18 19 20 21 22 23 24 25 26 27
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
chain bonds :
2-18 3-17 4-16 8-24 14-19 19-20 20-21 20-22 20-23 24-25 25-26 25-27
ring bonds :
1-2 1-6 2-3 3-4 4-7 5-6 5-9 6-7 7-11 8-10 8-9 10-11 10-15 11-12 12-13
13-14 14-15
exact/norm bonds :
2-18 3-17 4-16 8-24 14-19 19-20 20-21 20-22 20-23 24-25 25-27
exact bonds :
5-6 5-9 7-11 8-10 8-9 25-26
normalized bonds :
1-2 1-6 2-3 3-4 4-7 6-7 10-11 10-15 11-12 12-13 13-14 14-15
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS

Stereo Bonds:

24-8 (Single Wedge).

Stereo Chiral Centers:

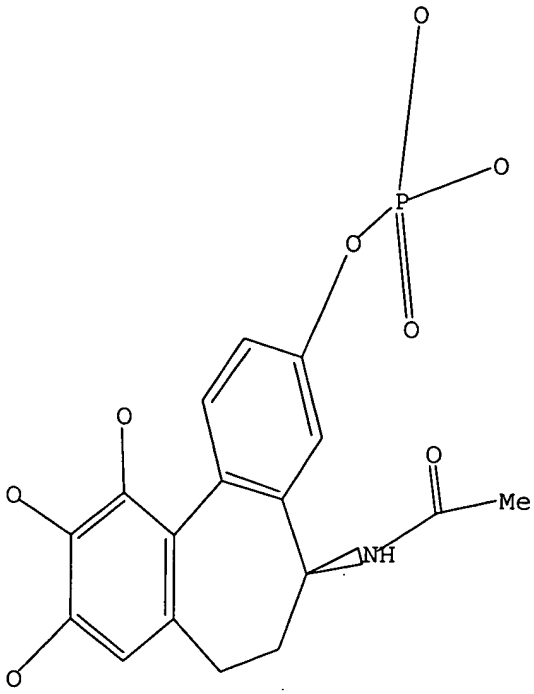
8 (Parity=Don't Care)

Stereo RSS Sets:

Type=Relative (Default). 1 Nodes= 8

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 10:22:03 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2 TO 124
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 10:22:08 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 22 TO ITERATE

100.0% PROCESSED 22 ITERATIONS 13 ANSWERS
SEARCH TIME: 00.00.01

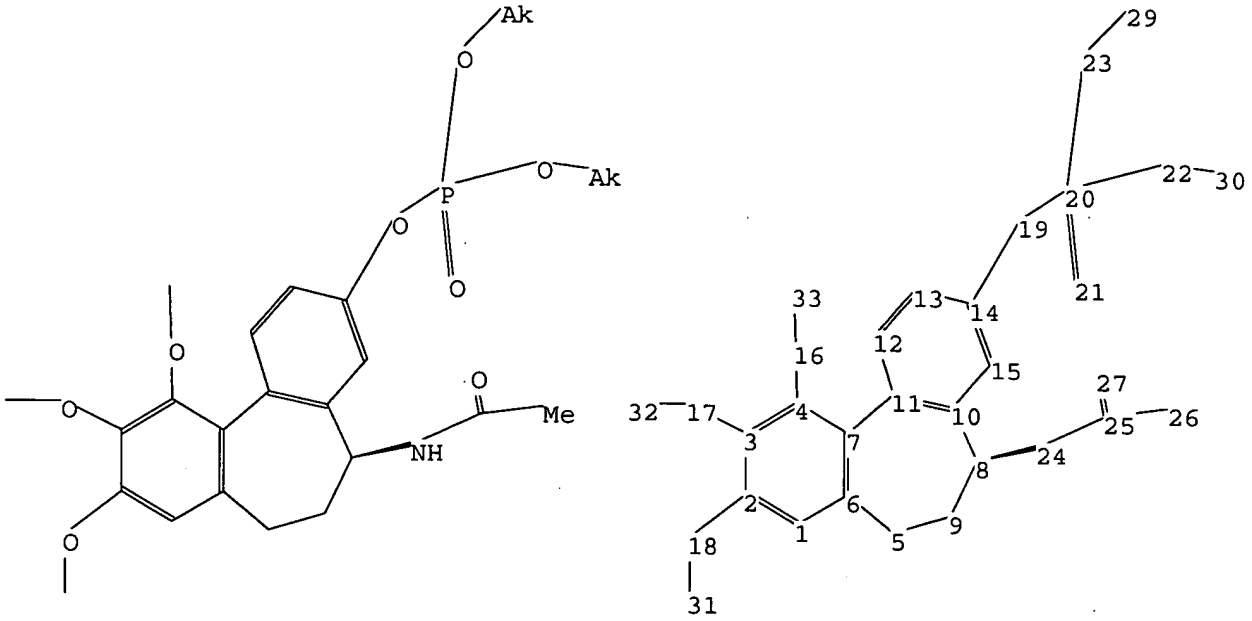
L3 13 SEA SSS FUL L1

```
=> FIL HCAPLUS
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       161.33     161.54

FILE 'HCAPLUS' ENTERED AT 10:22:14 ON 29 NOV 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 29 Nov 2005  VOL 143 ISS 23
FILE LAST UPDATED: 28 Nov 2005  (20051128/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s l3
L4          46 L3

=> FIL REGISTRY
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         9.80     171.34

FILE 'REGISTRY' ENTERED AT 10:24:35 ON 29 NOV 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   28 NOV 2005  HIGHEST RN 868827-82-1
DICTIONARY FILE UPDATES:  28 NOV 2005  HIGHEST RN 868827-82-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

*************************************************************************
*                                                                       *
* The CA roles and document type information have been removed from *
```

```
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10731842a.str
```




```
chain nodes :
16  17  18  19  20  21  22  23  24  25  26  27  29  30  31  32  33
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15
chain bonds :
2-18  3-17  4-16  8-24  14-19  16-33  17-32  18-31  19-20  20-21  20-22  20-23
22-30  23-29  24-25  25-26  25-27
ring bonds :
1-2  1-6  2-3  3-4  4-7  5-6  5-9  6-7  7-11  8-10  8-9  10-11  10-15  11-12  12-13
 13-14  14-15
exact/norm bonds :
2-18  3-17  4-16  8-24  14-19  16-33  17-32  18-31  19-20  20-21  20-22  20-23
22-30  23-29  24-25  25-27
```

exact bonds :
5-6 5-9 7-11 8-10 8-9 25-26
normalized bonds :
1-2 1-6 2-3 3-4 4-7 6-7 10-11 10-15 11-12 12-13 13-14 14-15
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS

Stereo Bonds:

24-8 (Single Wedge).

Stereo Chiral Centers:

8 (Parity=Don't Care)

Stereo RSS Sets:

Type=Relative (Default). 1 Nodes= 8

L5 STRUCTURE UPLOADED

=> d l5
L5 HAS NO ANSWERS
L5 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l5
SAMPLE SEARCH INITIATED 10:25:00 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2 TO 124
PROJECTED ANSWERS: 0 TO 0

L6 0 SEA SSS SAM L5

=> s l5 sss full
FULL SEARCH INITIATED 10:25:07 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 22 TO ITERATE

100.0% PROCESSED 22 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

L7 2 SEA SSS FUL L5

=> FIL HCAPLUS
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	161.33	332.67

FILE 'HCAPLUS' ENTERED AT 10:25:12 ON 29 NOV 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 29 Nov 2005 VOL 143 ISS 23
FILE LAST UPDATED: 28 Nov 2005 (20051128/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l7
L8 2 L7

=> d his

(FILE 'HOME' ENTERED AT 10:21:31 ON 29 NOV 2005)

FILE 'REGISTRY' ENTERED AT 10:21:46 ON 29 NOV 2005
L1 STRUCTURE UPLOADED
L2 1 S L1
L3 13 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 10:22:14 ON 29 NOV 2005
L4 46 S L3

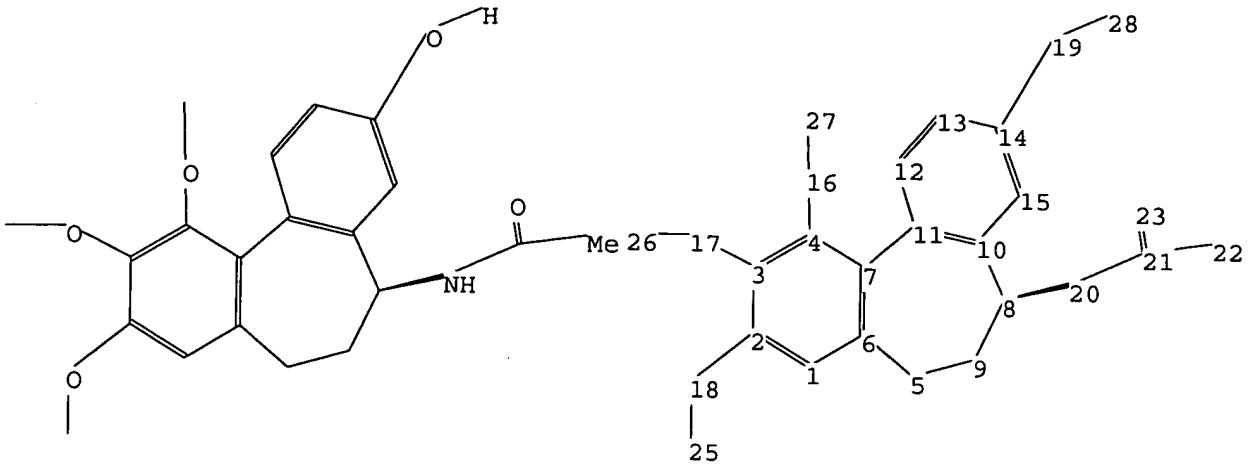
FILE 'REGISTRY' ENTERED AT 10:24:35 ON 29 NOV 2005
L5 STRUCTURE UPLOADED
L6 0 S L5
L7 2 S L5 SSS FULL

FILE 'HCAPLUS' ENTERED AT 10:25:12 ON 29 NOV 2005
L8 2 S L7

=> s 18
L9 2 L7

=> s 14
L10 46 L3

```
=> FIL REGISTRY
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY     SESSION
FULL ESTIMATED COST                                   12.25      344.92

FILE 'REGISTRY' ENTERED AT 10:28:11 ON 29 NOV 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   28 NOV 2005  HIGHEST RN 868827-82-1
DICTIONARY FILE UPDATES:  28 NOV 2005  HIGHEST RN 868827-82-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10731842b.str
```



chain nodes :
16 17 18 19 20 21 22 23 25 26 27 28
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
chain bonds :
2-18 3-17 4-16 8-20 14-19 16-27 17-26 18-25 19-28 20-21 21-22 21-23
ring bonds :
1-2 1-6 2-3 3-4 4-7 5-6 5-9 6-7 7-11 8-10 8-9 10-11 10-15 11-12 12-13
13-14 14-15
exact/norm bonds :
2-18 3-17 4-16 8-20 14-19 16-27 17-26 18-25 20-21 21-23
exact bonds :
5-6 5-9 7-11 8-10 8-9 19-28 21-22
normalized bonds :
1-2 1-6 2-3 3-4 4-7 6-7 10-11 10-15 11-12 12-13 13-14 14-15
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS

Stereo Bonds:

20-8 (Single Wedge).

Stereo Chiral Centers:

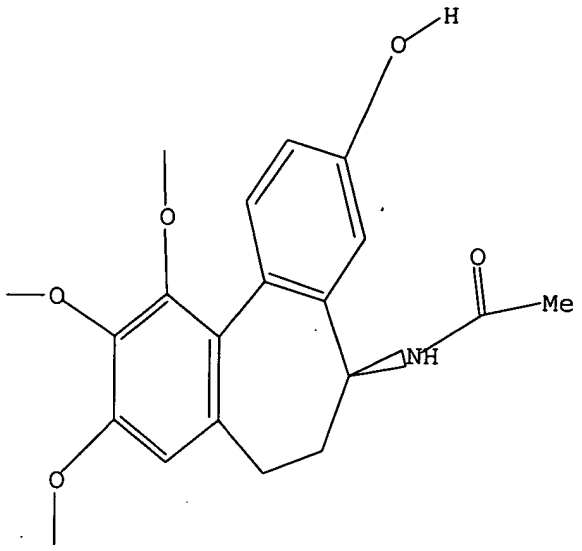
8 (Parity=Don't Care)

Stereo RSS Sets:

Type=Relative (Default). 1 Nodes= 8

L11 STRUCTURE UPLOADED

```
=> d l11
L11 HAS NO ANSWERS
L11             STR
```



Structure attributes must be viewed using STN Express query preparation.

```
=> s l11
SAMPLE SEARCH INITIATED 10:28:36 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        6 TO ITERATE

100.0% PROCESSED         6 ITERATIONS                                1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            6 TO      266
PROJECTED ANSWERS:               1 TO       80

L12           1 SEA SSS SAM L11

=> s l11 sss full
FULL SEARCH INITIATED 10:28:46 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      164 TO ITERATE.

100.0% PROCESSED       164 ITERATIONS                              11 ANSWERS
SEARCH TIME: 00.00.01

L13          11 SEA SSS FUL L11

=> FIL HCAPLUS
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             161.33     506.25

FILE 'HCAPLUS' ENTERED AT 10:28:52 ON 29 NOV 2005
```

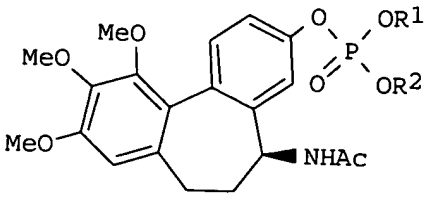
FILE COVERS 1907 - 29 Nov 2005 VOL 143 ISS 23
FILE LAST UPDATED: 28 Nov 2005 (20051128/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

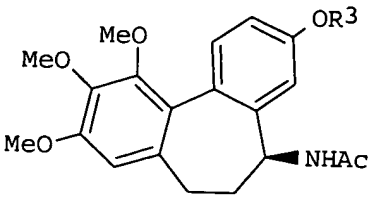
This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l13
L14           45 L13

=> d his

     (FILE 'HOME' ENTERED AT 10:21:31 ON 29 NOV 2005)

     FILE 'REGISTRY' ENTERED AT 10:21:46 ON 29 NOV 2005
L1                STRUCTURE UPLOADED
L2              1 S L1
L3             13 S L1 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 10:22:14 ON 29 NOV 2005
L4             46 S L3

     FILE 'REGISTRY' ENTERED AT 10:24:35 ON 29 NOV 2005
L5                STRUCTURE UPLOADED
L6              0 S L5
L7              2 S L5 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 10:25:12 ON 29 NOV 2005
L8              2 S L7
L9              2 S L8
L10            46 S L4

     FILE 'REGISTRY' ENTERED AT 10:28:11 ON 29 NOV 2005
L11               STRUCTURE UPLOADED
L12             1 S L11
L13            11 S L11 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 10:28:52 ON 29 NOV 2005
L14            45 S L13

=> s l10 and py<=2002
      22790426 PY<=2002
L15           12 L10 AND PY<=2002
```

```
=> s l14 and py<=2002
      22790426 PY<=2002
L16           40 L14 AND PY<=2002

=> s l16 and process
        2174213 PROCESS
        1459075 PROCESSES
        3237736 PROCESS
                  (PROCESS OR PROCESSES)
L17            0 L16 AND PROCESS

=> s l15 and process
        2174213 PROCESS
        1459075 PROCESSES
        3237736 PROCESS
                  (PROCESS OR PROCESSES)
L18            0 L15 AND PROCESS

=> d l8 ibib abs hitstr tot

L8   ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:472094  HCAPLUS
DOCUMENT NUMBER:          141:38765
TITLE:                    Process for the preparation of colchicine derivatives
                          and use of products obtained by this process
INVENTOR(S):              Wehrey, Christian; Droux, Serge
PATENT ASSIGNEE(S):       Aventis Pharma Sa, Fr.
SOURCE:                   Fr. Demande, 21 pp.
                          CODEN: FRXXBL
DOCUMENT TYPE:            Patent
LANGUAGE:                 French
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     FR 2848212            A1    20040611    FR 2002-15418            20021206
     WO 2004052895         A1    20040624    WO 2003-FR3585           20031204
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
             TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     EP 1569946            A1    20050907    EP 2003-796156           20031204
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     US 2004138182         A1    20040715    US 2003-731842           20031205
PRIORITY APPLN. INFO.:                       FR 2002-15418        A   20021206
                                             WO 2003-FR3585       W   20031204
OTHER SOURCE(S):          CASREACT 141:38765; MARPAT 141:38765
GI
```



I



II

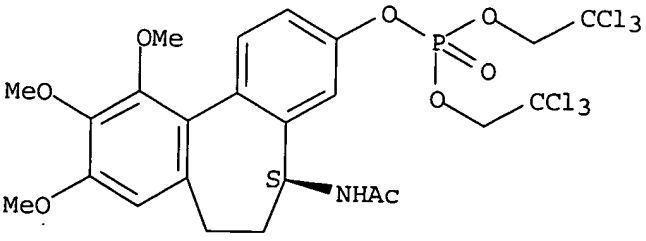
AB Method of preparation of colchicine derivs. I [R1, R2 = H, (un)substituted alkyl (especially, CH2CCl3), cycloalkyl, metal cation (Li, Na, K)] and their pharmaceutically acceptable salts, is characterized by phosphorylation of colchicine derivative II (R3 = H, labile substituents) with R4P(:O)(OR1)(OR2) [R4 = labile substituents (e.g., Cl, Br, I)] in the presence of a non-aromatic trialkylamine. Thus, sodium phosphate I (R1 = R2 = Na) was prepared from colchicine via ring contraction with I2 and NaOH in H2O, deiodination with Zn in AcOH, phosphorylation with (CCl3CH2O)2P(:O)Cl in CH2Cl2 containing Et3N, deesterification with Zn-Cu amalgam in DMF and salt formation with aqueous NaOH. The invention relates to primarily a method of preparation of organophosphores compds. and their salts, having a therapeutic activity, in particular in oncol. (no data).

IT **701232-77-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and deesterification of; process for the preparation of colchicine
derivs. and use of as a therapeutic for oncol.)

RN 701232-77-1 HCAPLUS

CN Phosphoric acid, (5S)-5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-5H-dibenzo[a,c]cyclohepten-3-yl bis(2,2,2-trichloroethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:64693 HCAPLUS
DOCUMENT NUMBER: 130:125254
TITLE: Preparation and formulation of colchinol derivs. useful for treatment of diseases involving angiogenesis

INVENTOR(S): Dougherty, Graeme
PATENT ASSIGNEE(S): Angiogene Pharmaceuticals Ltd., UK
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2

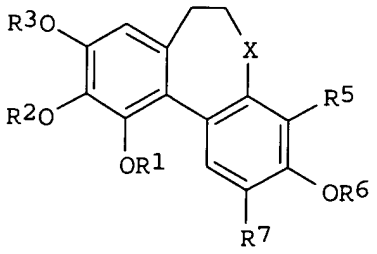
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902166	A1	19990121	WO 1998-GB1977	19980706
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2292549	AA	19990121	CA 1998-2292549	19980706
AU 9882311	A1	19990208	AU 1998-82311	19980706
AU 741213	B2	20011129		
EP 1001785	A1	20000524	EP 1998-932374	19980706
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9810681	A	20000815	BR 1998-10681	19980706
TR 9903149	T2	20000921	TR 1999-9903149	19980706
NZ 501341	A	20010831	NZ 1998-501341	19980706
JP 2001515516	T2	20010918	JP 1999-508313	19980706
JP 3455549	B2	20031014		
RU 2232021	C2	20040710	RU 2000-102889	19980706
ZA 9900106	A	19990707	ZA 1999-106	19990107
MX 9911154	A	20000930	MX 1999-11154	19991202
US 6423753	B1	20020723	US 2000-477805	20000105
NO 2000000077	A	20000107	NO 2000-77	20000107

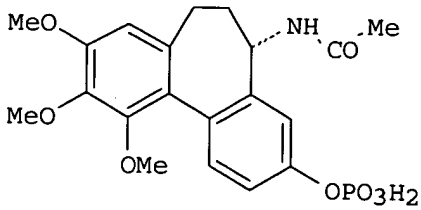
PRIORITY APPLN. INFO.:

GB 1997-14249	A	19970708
WO 1998-GB1977	W	19980706

OTHER SOURCE(S): MARPAT 130:125254
GI



I



II

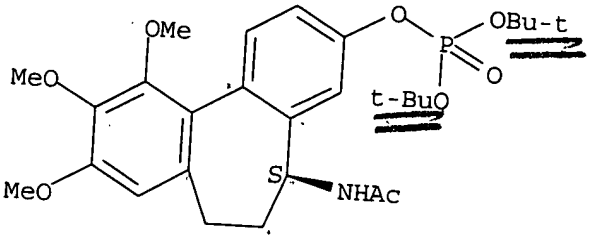
AB Colchinol derivs. I [R1, R2, R3, R6 = H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, alkanoyl, PO3H2; R5, R7 = H, alkyl, halogen, hydroxy, alkoxy, nitro, amino; X = CO, CS, CH2, CHR4, NR8R9; R4 = OH, alkoxy; R8 = H, alkyl, cycloalkyl, alkanoyl, thioalkanoyl, aryl, heteroaryl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, aryloxycarbonyl,

aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, alkylsulfonyl, arylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl or arylaminosulfonyl; R9 = H, alkyl, cycloalkyl] were prepared and formulated for treatment of diseases involving angiogenesis. Thus, phosphate II was prepared via sequential O-phosphorylation of N-acetylcolchinol with (Me3CO)2PNEt2, P oxidation with MCPBA, and deesterification with TFA. The prepared compds were tested for activity against turmor vasculature with the compds. having R6 = OPO3H2 as most preferred.

IT **219923-15-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and formulation of colchinol derivs. useful for treatment of diseases involving angiogenesis)

RN 219923-15-6 HCAPLUS
CN Phosphoric acid, (5S)-5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-5H-dibenzo[a,c]cyclohepten-3-yl bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l9 ibib abs hitstr tot

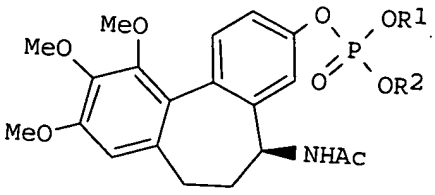
L9 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:472094 HCAPLUS
DOCUMENT NUMBER: 141:38765
TITLE: Process for the preparation of colchicine derivatives and use of products obtained by this process
INVENTOR(S): Wehrey, Christian; Droux, Serge
PATENT ASSIGNEE(S): Aventis Pharma Sa, Fr.
SOURCE: Fr. Demande, 21 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2848212	A1	20040611	FR 2002-15418	20021206
WO 2004052895	A1	20040624	WO 2003-FR3585	20031204

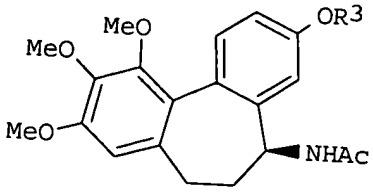
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,

OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1569946 A1 20050907 EP 2003-796156 20031204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 2004138182 A1 20040715 US 2003-731842 20031205
PRIORITY APPLN. INFO.: FR 2002-15418 A 20021206
WO 2003-FR3585 W 20031204

OTHER SOURCE(S): CASREACT 141:38765; MARPAT 141:38765
GI



I



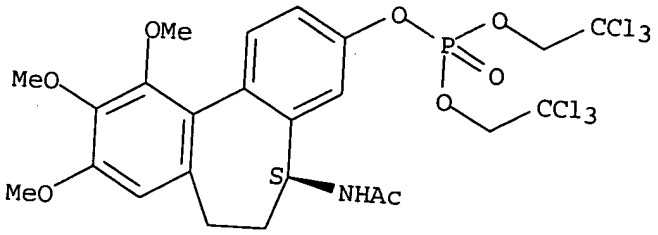
II

AB Method of preparation of colchicine derivs. I [R1, R2 = H, (un)substituted alkyl (especially, CH2CCl3), cycloalkyl, metal cation (Li, Na, K)] and their pharmaceutically acceptable salts, is characterized by phosphorylation of colchicine derivative II (R3 = H, labile substituents) with R4P(:O)(OR1)(OR2) [R4 = labile substituents (e.g., Cl, Br, I)] in the presence of a non-aromatic trialkylamine. Thus, sodium phosphate I (R1 = R2 = Na) was prepared from colchicine via ring contraction with I2 and NaOH in H2O, deiodination with Zn in AcOH, phosphorylation with (CCl3CH2O)2P(:O)Cl in CH2Cl2 containing Et3N, deesterification with Zn-Cu amalgam in DMF and salt formation with aqueous NaOH. The invention relates to primarily a method of preparation of organophosphores compds. and their salts, having a therapeutic activity, in particular in oncol. (no data).

IT **701232-77-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and deesterification of; process for the preparation of colchicine
derivs. and use of as a therapeutic for oncol.)

RN 701232-77-1 HCAPLUS
CN Phosphoric acid, (5S)-5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-5H-dibenzo[a,c]cyclohepten-3-yl bis(2,2,2-trichloroethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

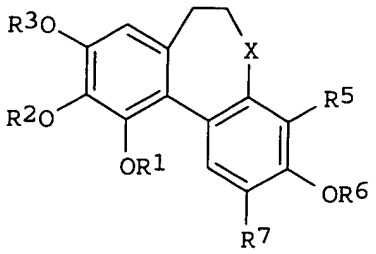
L9 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:64693 HCAPLUS
DOCUMENT NUMBER: 130:125254
TITLE: Preparation and formulation of colchinol derivs. useful for treatment of diseases involving angiogenesis
INVENTOR(S): Dougherty, Graeme
PATENT ASSIGNEE(S): Angiogene Pharmaceuticals Ltd., UK
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902166	A1	19990121	WO 1998-GB1977	19980706
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2292549	AA	19990121	CA 1998-2292549	19980706
AU 9882311	A1	19990208	AU 1998-82311	19980706
AU 741213	B2	20011129		
EP 1001785	A1	20000524	EP 1998-932374	19980706
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9810681	A	20000815	BR 1998-10681	19980706
TR 9903149	T2	20000921	TR 1999-9903149	19980706
NZ 501341	A	20010831	NZ 1998-501341	19980706
JP 2001515516	T2	20010918	JP 1999-508313	19980706
JP 3455549	B2	20031014		
RU 2232021	C2	20040710	RU 2000-102889	19980706
ZA 9900106	A	19990707	ZA 1999-106	19990107
MX 9911154	A	20000930	MX 1999-11154	19991202
US 6423753	B1	20020723	US 2000-477805	20000105
NO 2000000077	A	20000107	NO 2000-77	20000107

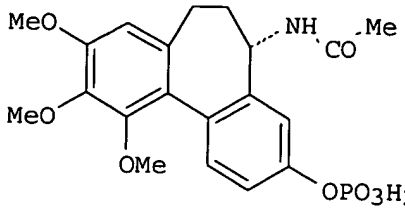
PRIORITY APPLN. INFO.: GB 1997-14249 A 19970708
WO 1998-GB1977 W 19980706

OTHER SOURCE(S): MARPAT 130:125254

GI



I



II

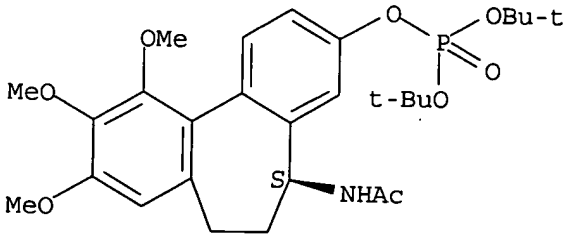
AB Colchinol derivs. I [R1, R2, R3, R6 = H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, alkanoyl, PO3H2; R5, R7 = H, alkyl, halogen, hydroxy, alkoxy, nitro, amino; X = CO, CS, CH2, CHR4, NR8R9; R4 = OH, alkoxy; R8 = H, alkyl, cycloalkyl, alkanoyl, thioalkanoyl, aryl, heteroaryl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, alkylsulfonyl, arylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl or arylaminosulfonyl; R9 = H, alkyl, cycloalkyl] were prepared and formulated for treatment of diseases involving angiogenesis. Thus, phosphate II was prepared via sequential O-phosphorylation of N-acetylcolchinol with (Me3CO)2PNEt2, P oxidation with MCPBA, and deesterification with TFA. The prepared compds were tested for activity against turmor vasculature with the compds. having R6 = OPO3H2 as most preferred.

IT **219923-15-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and formulation of colchinol derivs. useful for treatment of diseases involving angiogenesis)

RN 219923-15-6 HCAPLUS

CN Phosphoric acid, (5S)-5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-5H-dibenzo[a,c]cyclohepten-3-yl bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l15 ibib abs hitstr tot

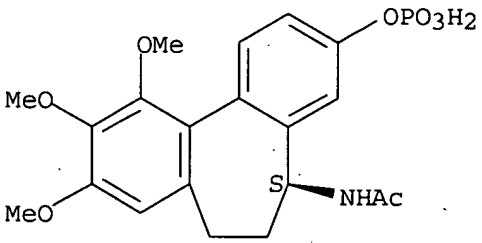
L15 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:338824 HCAPLUS

DOCUMENT NUMBER: 141:306954
TITLE: Microbubble destruction-reperfusion in the non-invasive measurement of the vascular targeting effects of the anti-cancer drug ZD6126
AUTHOR(S): Karshafian, Raffi; Burns, Peter N.; Qi, Xiuling; Zhang, Ming Yu
CORPORATE SOURCE: Department of Medical Biophysics, Sunnybrook & Women's College Health Sciences Centre, University of Toronto, Toronto, ON, M4N 3M5, Can.
SOURCE: Proceedings - IEEE Ultrasonics Symposium (**2002**), (Vol. 2), 1989-1992
CODEN: PIEUEZ; ISSN: 1051-0117
PUBLISHER: Institute of Electrical and Electronics Engineers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A combination of microbubble destruction-reperfusion flow measurement and real time contrast imaging was used to assess the effects of an anti-vascular agent ZD6126 on exptl. VX-2 tumors in the rabbit. Results of dose-response study suggest that 30 mg/kg is an appropriate dose of drug in rabbits. The initial results of the longitudinal study suggest that there is an initial significant drop in flow and volume at around 4 h following injection of the anti-vascular drug ZD6126, followed by a recovery that is complete by 72 h. Pulse inversion contrast imaging with the microbubble agent provided quant. monitoring of blood flow and blood volume of tumors undergoing anti-vascular therapy. This method may be suitable for use in clin. trials of anti-vascular and anti-angiogenic therapies, providing a unique method for the non-invasive monitoring of hemodynamic effect in superficial tumors such as those in breast cancer.

IT **219923-05-4**, ZD6126
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microbubble destruction-reperfusion in non-invasive measurement of vascular targeting effects of anti-cancer drug ZD6126)
RN 219923-05-4 HCAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-9,10,11-trimethoxy-3-(phosphonooxy)-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

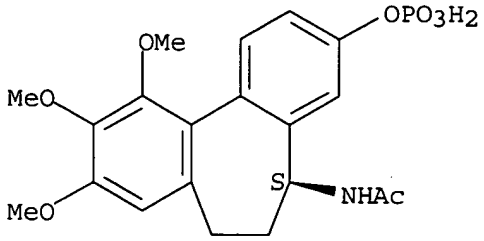


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:145065 HCAPLUS
DOCUMENT NUMBER: 139:288187
TITLE: Enhancement of radiation therapy by vascular targeting agents
AUTHOR(S): Siemann, Dietmar W.; Horsman, Michael R.
CORPORATE SOURCE: Department of Radiation Oncology, University of

Florida Shands Cancer Center, Gainesville, FL, 32610, USA
SOURCE: Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2002), 3(11), 1660-1665
CODEN: COIDAZ; ISSN: 1472-4472
PUBLISHER: PharmaPress Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The tumor vessel support network offers a tantalizing target for cancer therapy, given the complete dependence of a solid neoplasia on the vasculature for both the delivery of oxygen and other nutrients, as well as the effective removal of waste products. Attacking a tumor's supportive blood vessel network offers a means of improving cancer cure rates on the basis of two principles. The first reflects evidence indicating that physiol. conditions in tumors, arising primarily as a consequence of inadequate and nonuniform vascular networks, are significant contributors to resistance to non-surgical anticancer treatments. The second involves the recognition that the inherent differences between blood vessels in tumors and those associated with normal tissues provide a variety of unique targets for the design of novel therapeutics, highly selective for neoplastic growth. Therapeutic approaches that aim to destroy the tumor endothelium are being actively pursued. The application of such vascular targeting strategies as adjuvants to conventional therapeutics such as radiotherapy, offers unique opportunities to develop even more effective cancer therapies.
IT **219923-05-4**, ZD-6126
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancement of radiation therapy by vascular targeting agents)
RN 219923-05-4 HCAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-9,10,11-trimethoxy-3-(phosphonooxy)-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:10896 HCAPLUS
DOCUMENT NUMBER: 139:46518
TITLE: ZD6126: a novel vascular-targeting agent that causes selective destruction of tumor vasculature
AUTHOR(S): Davis, Peter D.; Dougherty, Graeme J.; Blakey, David C.; Galbraith, Susan M.; Tozer, Gillian M.; Holder, Angela L.; Naylor, Matthew A.; Nolan, John; Stratford, Michael R. L.; Chaplin, David J.; Hill, Sally A.
CORPORATE SOURCE: Oxford Science Park, Angiogene Pharmaceuticals Ltd., Oxford, OX4 4GA, UK

SOURCE: Cancer Research (**2002**), 62(24), 7247-7253
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

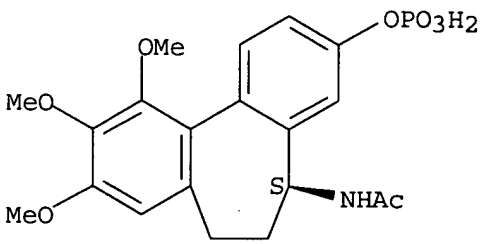
AB Physiol. differences between tumor and normal vasculature provide a target for drug discovery. In particular, the immature nature of tumor vasculature may render it intrinsically sensitive to disruption by agents affecting the endothelial cell cytoskeleton, including tubulin-binding agents. In this article, we report the synthesis of a water-soluble phosphate prodrug, ZD6126, of the tubulin-binding agent N-acetylcolchinol. In vitro studies demonstrate the comparative tubulin-binding properties of the prodrug and active drug, and show the induction of pronounced, reversible changes in endothelial cell morphol. at subcytotoxic doses. Neither ZD6126 nor N-acetylcolchinol showed effects on the growth of human umbilical vein endothelial cells at concns. below 100 μM. In contrast, changes in endothelial cell morphol. were seen at much lower, noncytotoxic concns. (0.1 μM) of ZD6126 and more pronounced effects were seen in proliferating vs. confluent endothelial cell cultures. In vivo studies were carried out using a murine tumor model (CaNT) with single administration of a dose well below the maximum tolerated dose. These studies showed a large reduction in vascular volume, induction of extensive necrosis in tumors, and a reduced tumor cell yield in a clonal excision assay, consistent with vascular rather than cytotoxic effects. A viable rim of tumor remained after single-dose administration and minimal growth delay was observed However, well-tolerated, multiple administration regimens led to pronounced tumor-growth delay. In the human xenograft FaDu, the growth delay given by a single dose of paclitaxel was enhanced by combination with a single dose of ZD6126, and the growth delay given by the combination was greater than the sum of the growth delays from the individual treatments. These findings show that ZD6126 is a promising antivascular agent for the treatment of solid tumors.

IT **219923-05-4P**, ZD6126
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ZD6126, a novel vascular-targeting agent that causes selective destruction of tumor vasculature)

RN 219923-05-4 HCAPLUS

CN Acetamide, N-[(5S)-6,7-dihydro-9,10,11-trimethoxy-3-(phosphonooxy)-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

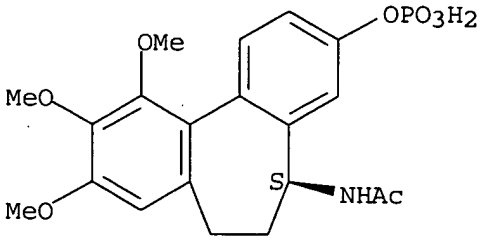
L15 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:897676 HCAPLUS

DOCUMENT NUMBER: 138:362290
TITLE: High-frequency Doppler ultrasound monitors the effects of antivascular therapy on tumor blood flow
AUTHOR(S): Goertz, David E.; Yu, Joanne L.; Kerbel, Robert S.; Burns, Peter N.; Foster, F. Stuart
CORPORATE SOURCE: Sunnybrook and Women's College Health Sciences Centre, Department of Medical Biophysics, University of Toronto, Toronto, ON, M4N 3M5, Can.
SOURCE: Cancer Research (**2002**), 62(22), 6371-6375
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of antivascular therapy on blood flow in superficial tumors was monitored using novel high frequency Doppler (HFD) ultrasound techniques. Human melanoma cells (MeWo) were injected orthotopically into the skin of athymic nude mice. Volumetric HFD imaging of established melanomas detected a significant reduction in blood flow 4 h after injection of the tumor vascular targeting agent ZD6126 followed by a recovery of flow by 24 h after injection. Measurements of tumor perfusion in situ by Hoechst 33342 staining correlated with the ultrasound results. This study demonstrates the feasibility of HFD as a noninvasive, quant. tool for following longitudinally the effects of antivascular therapy on blood flow in superficial tumors.

IT **219923-05-4**, ZD6126
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high-frequency Doppler ultrasound monitors the effects of antivascular therapy on tumor blood flow)
RN 219923-05-4 HCAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-9,10,11-trimethoxy-3-(phosphonooxy)-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:896039 HCAPLUS
DOCUMENT NUMBER: 139:316716
TITLE: Antitumor efficacy of conventional anticancer drugs is enhanced by the vascular targeting agent ZD6126
AUTHOR(S): Siemann, Dietmar W.; Rojiani, Amyn M.
CORPORATE SOURCE: Shands Cancer Center, Department of Radiation Oncology, University of Florida, Gainesville, FL, 32606, USA
SOURCE: International Journal of Radiation Oncology, Biology, Physics (**2002**), 54(5), 1512-1517

CODEN: IOBPD3; ISSN: 0360-3016
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

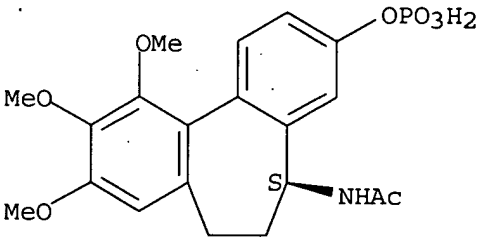
AB Purpose: The present report reviews the preclin. data on combined chemotherapy/vascular targeting agent treatments. Basic principles are illustrated in studies evaluating the antitumor efficacy of the vascular targeting agent ZD6126 (N-acetylcochinol-O-phosphate) when combined with the anticancer drug cisplatin in exptl. rodent (KHT sarcoma) and human renal (Caki-1) tumor models. Methods and Materials: C3H/HeJ and NCR/nu-nu mice bearing i.m. tumors were injected i.p. with ZD6126 (0-150 mg/kg) or cisplatin (0-20 mg/kg) either alone or in combination. Tumor response to treatment was assessed by clonogenic cell survival. Results: Treatment with ZD6126 was found to damage existing neovasculature, leading to a rapid vascular shutdown. Histol. evaluation showed dose-dependent morphol. damage of tumor cells within a few hours after drug exposure, followed by extensive central tumor necrosis and neoplastic cell death as a result of prolonged ischemia. ZD6126 doses that led to pathophysiol. effects also enhanced the tumor cell killing of cisplatin when administered either 24 h before or 1-24 h after chemotherapy. In both tumor models, the administration of a 150 mg/kg dose of ZD6126 1 h after a range of doses of cisplatin resulted in an increase in tumor cell kill 10-500-fold greater than that seen with chemotherapy alone. In contrast, the inclusion of the antivascular agent did not increase bone marrow stem cell toxicity associated with this anticancer drug. Conclusion: The results obtained in the KHT and Caki-1 tumor models indicate that ZD6126 effectively enhanced the antitumor effects of cisplatin therapy. These findings are representative of the marked enhancements generally observed when vascular targeting agents are combined with chemotherapy in solid tumor therapy.

IT **219923-05-4**, ZD6126
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vascular targeting agent ZD6126 enhancement of cisplatin antitumor efficacy but not hemotoxicity)

RN 219923-05-4 HCAPLUS

CN Acetamide, N-[(5S)-6,7-dihydro-9,10,11-trimethoxy-3-(phosphonooxy)-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

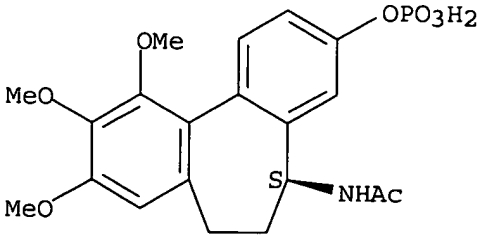


REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:524893 HCAPLUS
DOCUMENT NUMBER: 138:83042
TITLE: Antitumor activity of the novel vascular targeting agent ZD6126 in a panel of tumor models

AUTHOR(S): Blakey, David C.; Westwood, F. Russell; Walker, Mike; Hughes, Gareth D.; Davis, Peter D.; Ashton, Sue E.; Ryan, Anderson J.
CORPORATE SOURCE: Cancer and Infection Bioscience Department, AstraZeneca, Cheshire, SK10 4TG, UK
SOURCE: Clinical Cancer Research (**2002**), 8(6), 1974-1983
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to examine the antitumor effects of the novel vascular targeting agent ZD6126 and to use histol., CD31 immunohistochem., and electron microscopy to gain an insight into the mechanism of action of this novel agent. The antitumor effects of ZD6126 were examined using a range of solid tumor models: (a) ras-transformed mouse 3T3 fibroblasts (Hras5); and (b) human lung (Calu-6), colorectal (LoVo and HT-29), prostate (PC-3), ovarian (SKOV-3), and breast (MDA-MB-231) tumors, grown as xenografts in nude mice. In vivo, a well-tolerated dose of ZD6126 was shown to cause rapid effects on tumor endothelium leading to exposure of the basal lamina after cell retraction and subsequent loss of endothelial cells. This led to thrombosis and vessel occlusion, resulting in extensive tumor necrosis 24 h after ZD6126 administration. Dose-response studies showed that these effects were seen at a dose 8- to 16-fold lower than the maximum tolerated dose, demonstrating that ZD6126 has a wide therapeutic margin in these mouse models. A single dose of ZD6126 (200 mg/kg) led to a significant growth delay in Calu-6 and LoVo tumors. Growth delay was increased when 100 mg/kg ZD6126 was given as a well-tolerated regime in five daily doses. Finally, combining ZD6126 with cisplatin resulted in greater than additive enhancement in growth delay in the Calu-6 model. These findings provide direct support that ZD6126 selectively disrupts tumor vasculature, demonstrate that it has activity in a range of tumor xenograft models, and show that it can significantly enhance the antitumor efficacy of cisplatin.
IT **219923-05-4**, ZD6126
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor activity of novel vascular targeting agent ZD6126 in panel of tumor models)
RN 219923-05-4 HCAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-9,10,11-trimethoxy-3-(phosphonooxy)-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

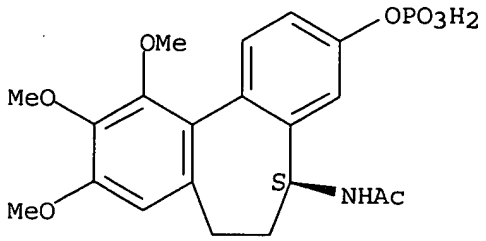
L15 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:519072 HCAPLUS
DOCUMENT NUMBER: 138:83027
TITLE: Activity of a new vascular targeting agent, ZD6126, in pulmonary metastases by human lung adenocarcinoma in nude mice
AUTHOR(S): Goto, Hisatsugu; Yano, Seiji; Zhang, Helong; Matsumori, Yuka; Ogawa, Hirohisa; Blakey, David C.; Sone, Saburo
CORPORATE SOURCE: Department of Internal Medicine and Molecular Therapeutics, Course of Medical Oncology, The University of Tokushima School of Medicine, Tokushima, 770-8503, Japan
SOURCE: Cancer Research (**2002**), 62(13), 3711-3715
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB ZD6126 (ANG453) is a novel vascular targeting agent that selectively disrupts the cytoskeleton of endothelial cells in tumor. In mouse s.c. xenograft models, ZD6126 was found to induce selective occlusion of tumor blood vessels, cessation of tumor blood flow, and death of tumor cells because of the starvation of oxygen and nutrition. Here, we investigated whether ZD6126 inhibited the metastatic formation of human non-small cell lung cancer cells. PC14PE6 (adenocarcinoma) and H226 (squamous cell carcinoma) cells were injected into the tail vein of nude mice, and lung metastases were estimated ZD6126 treatment involved either a single dose on 24 h before killing or daily doses from day 14 until the end of the experiment Single treatment with i.p. injection of 200 mg/kg ZD6126 caused bleeding and necrotic changes in the tumor by 24 h. Histol. anal. revealed that apoptotic tumor cells were markedly increased in the ZD6126-treated group. Moreover, ZD6126 induced the apoptosis of CD31-pos. vascular endothelial cells in tumors but not in the normal lung parenchyma. When mice were treated daily with 100 mg/kg ZD6126 from day 14 until the end of the experiment, the lung weight was significantly less in the ZD6126-treated group than that of the control group, despite no difference in the number of metastatic nodules. These data suggest that ZD6126 could demonstrate its antitumor activity against both already established and early phase of lung cancer metastasis by causing the selective apoptosis of tumor endothelial cells and destruction of the tumor vasculature.

IT **219923-05-4**, ZD6126
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiogenesis inhibitor ZD6126 selectively targets human lung carcinoma metastases)
RN 219923-05-4 HCAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-9,10,11-trimethoxy-3-(phosphonooxy)-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

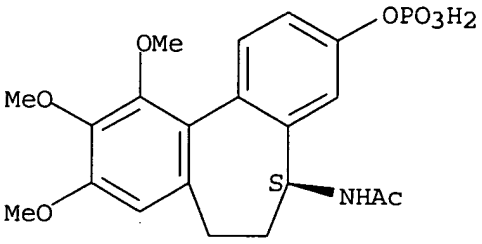


REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:339282 HCAPLUS
DOCUMENT NUMBER: 137:365619
TITLE: Enhancement of radiation therapy by the novel vascular targeting agent ZD6126
AUTHOR(S): Siemann, Dietmar W.; Rojiani, Amyn M.
CORPORATE SOURCE: Shands Cancer Center, Department of Radiation Oncology, University of Florida, Gainesville, FL, USA
SOURCE: International Journal of Radiation Oncology, Biology, Physics (**2002**), 53(1), 164-171
CODEN: IOBPD3; ISSN: 0360-3016
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: The aim of this study was to evaluate the antitumor efficacy of the novel vascular targeting agent ZD6126 (N-acetylcochinol-O-phosphate) in the rodent KHT sarcoma model, either alone or in combination with single- or fractionated-dose radiation therapy. Methods: C3H/HeJ mice bearing i.m. KHT tumors were injected i.p. with ZD6126 doses ranging from 10 to 150 mg/kg. Tumors were irradiated locally in unanesthetized mice using a linear accelerator. Tumor response to ZD6126 administered alone or in combination with radiation was assessed by clonogenic cell survival assay or tumor growth delay. Results:Treatment with ZD6126 led to a rapid tumor vascular shutdown as determined by Hoechst 33342 diffusion. Histol. evaluation showed morphol. damage of tumor cells within a few hours after drug exposure, followed by extensive central tumor necrosis and neoplastic cell death as a result of prolonged ischemia. When combined with radiation, a 150 mg/kg dose of ZD6126 reduced tumor cell survival 10-500-fold compared with radiation alone. These enhancements in tumor cell killing could be achieved for ZD6126 given both before and after radiation exposure. Further, the shape of the cell survival curve observed after the combination therapy suggested that including ZD6126 in the treatment had a major effect on the radiation-resistant hypoxic cell subpopulation associated with this tumor. Finally, when given on a once-weekly basis in conjunction with fractionated radiotherapy, ZD6126 treatment was found to significantly increase the tumor response to daily 2.5 Gy fractions. Conclusion: The present results demonstrated that in the KHT sarcoma, ZD6126 caused rapid tumor vascular shutdown, induction of central tumor necrosis, tumor cell death secondary to ischemia, and enhancement of the antitumor effects of radiation therapy.
IT **219923-05-4**, ZD 6126
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancement of sarcoma cell death by radiotherapy in combination with novel vascular targeting agent ZD6126)
RN 219923-05-4 HCAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-9,10,11-trimethoxy-3-(phosphonooxy)-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:747618 HCAPLUS
DOCUMENT NUMBER: 135:283181
TITLE: Divided dose therapies with vascular damaging activity
INVENTOR(S): Davis, Peter David
PATENT ASSIGNEE(S): Angiogene Pharmaceuticals Ltd., UK
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001074369	A1	20011011	WO 2001-GB1329		20010327 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2402078	AA	20011011	CA 2001-2402078		20010327 <--
EP 1272200	A1	20030108	EP 2001-915495		20010327
EP 1272200	B1	20050622			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001009671	A	20030204	BR 2001-9671		20010327
JP 2003528921	T2	20030930	JP 2001-572112		20010327
EE 200200549	A	20040216	EE 2002-549		20010327
AT 298240	E	20050715	AT 2001-915495		20010327
ZA 2002007108	A	20031204	ZA 2002-7108		20020904
ZA 2002007114	A	20040204	ZA 2002-7114		20020904
US 2003055024	A1	20030320	US 2002-239898		20020926
NO 2002004683	A	20021015	NO 2002-4683		20020930 <--
PRIORITY APPLN. INFO.:			GB 2000-7740	A	20000331
			GB 2000-13928	A	20000608
			GB 2000-14904	A	20000620
			WO 2001-GB1329	W	20010327

AB The invention discloses the use of a vascular damaging agent or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for administration in divided doses for use in the production of a vascular

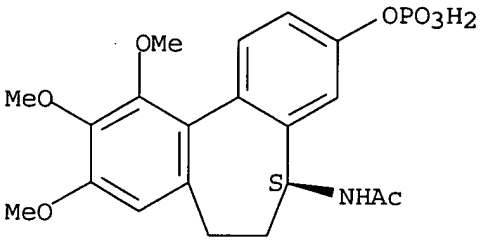
damaging effect in a warm-blooded animal such as a human. In particular the vascular damaging agent is ZD6126 (preparation described), or a pharmaceutically acceptable salt thereof. The invention also relates to methods of treatment using a vascular damaging agent in divided doses. The vascular damaging agents are useful in the treatment of tumors.

IT **219923-05-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(divided dose therapies with vascular damaging activity)

RN 219923-05-4 HCAPLUS

CN Acetamide, N-[(5S)-6,7-dihydro-9,10,11-trimethoxy-3-(phosphonooxy)-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:747617 HCAPLUS
DOCUMENT NUMBER: 135:283180
TITLE: Combination therapies using ZD6126 with a platinum antitumor agent, a taxane, or ionizing radiation for vascular damaging activity
INVENTOR(S): Davis, Peter David; Dougherty, Graeme
PATENT ASSIGNEE(S): Angiogene Pharmaceuticals Ltd., UK
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074368	A1	20011011	WO 2001-GB1317	20010327 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EE 200200565	A	20040615	EE 2002-565	20010227
CA 2402539	AA	20011011	CA 2001-2402539	20010327 <--
EP 1272199	A1	20030108	EP 2001-915490	20010327

EP 1272199	B1	20050119			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001009672	A	20030204	BR 2001-9672		20010327
JP 2003528920	T2	20030930	JP 2001-572111		20010327
AT 287267	E	20050215	AT 2001-915490		20010327
PT 1272199	T	20050531	PT 2001-915490		20010327
NZ 521025	A	20050624	NZ 2001-521025		20010327
ES 2236199	T3	20050716	ES 2001-1915490		20010327
ZA 2002007108	A	20031204	ZA 2002-7108		20020904
ZA 2002007114	A	20040204	ZA 2002-7114		20020904
NO 2002004646	A	20021015	NO 2002-4646		20020927 <--
US 2003166617	A1	20030904	US 2003-240213		20030404
US 6906048	B2	20050614			
~~US 2005107346~~	A1	20050519	US 2004-994639		20041123
PRIORITY APPLN. INFO.:			GB 2000-7740	A	20000331
			GB 2000-13927	A	20000608
			GB 2000-14908	A	20000620
			WO 2001-GB1317	W	20010327

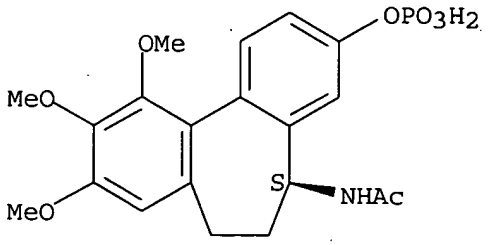
AB A method for the production of a vascular damaging effect in a warm-blooded animal, e.g. a human, comprises administering to the animal an effective amount of ZD6126 (preparation described), or a pharmaceutically acceptable salt thereof, before, after or simultaneously with an effective amount of one of the following therapies: (i) ionizing radiation; (ii) a platinum anti-tumor agent; and (iii) a taxane. The invention also relates to the use of ZD6126 and one of the above therapies in the manufacture of a medicament for use in the production of a vascular damaging effect in a warm-blooded animal, e.g. a human, and to pharmaceutical compns. and kits each comprising ZD6126 and one of a platinum anti-tumor agent and a taxane.

IT **219923-05-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ZD6126 combination with platinum antitumor agent, taxane, or ionizing radiation for vascular damaging activity)

RN 219923-05-4 HCAPLUS

CN Acetamide, N-[(5S)-6,7-dihydro-9,10,11-trimethoxy-3-(phosphonooxy)-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



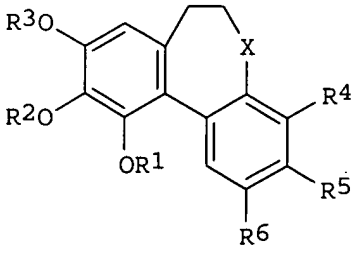
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:475616 HCAPLUS
DOCUMENT NUMBER: 133:89673
TITLE: Preparation of colchinol derivatives for use as vascular damaging agents

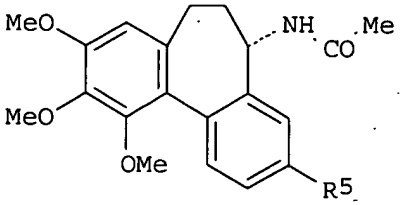
INVENTOR(S): Davis, Peter David; Arnould, Jean-Claude; Boyle, Francis Thomas
PATENT ASSIGNEE(S): Angiogene Pharmaceuticals Ltd., UK
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2000040529	A1	20000713	WO 1999-GB4436		19991224	<--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG						
CA 2355302	AA	20000713	CA 1999-2355302		19991224	<--
EP 1140745	A1	20011010	EP 1999-962468		19991224	<--
EP 1140745	B1	20031022				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO						
BR 9916790	A	20011204	BR 1999-16790		19991224	<--
JP 2002534400	T2	20021015	JP 2000-592241		19991224	<--
AU 760830	B2	20030522	AU 2000-18823		19991224	
AT 252529	E	20031115	AT 1999-962468		19991224	
NZ 512398	A	20031128	NZ 1999-512398		19991224	
PT 1140745	T	20040331	PT 1999-962468		19991224	
ES 2211206	T3	20040701	ES 1999-962468		19991224	
ZA 2001005065	A	20020920	ZA 2001-5065		20010620	<--
NO 2001003367	A	20010905	NO 2001-3367		20010706	<--
PRIORITY APPLN. INFO.:			GB 1999-334	A	19990107	
			WO 1999-GB4436	W	19991224	

OTHER SOURCE(S): MARPAT 133:89673
GI



I



II

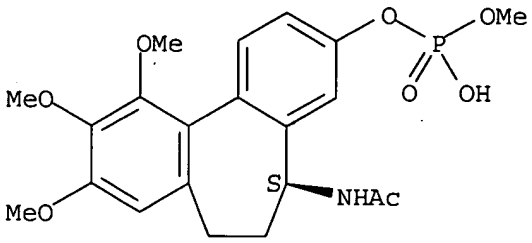
AB Colchinol derivs., such as I [X = CO, CS, C:NOH, CHR7, etc.; R1, R2, R3 = H, phosphate, sulfate, alkyl, etc.; R4, R5, R6 = H, OH, NO2, NH2, phosphate, phosphonate, halogen, carboxy, carbamoyl, acyl, etc.; R7 = H, OH, alkoxy, amino, acylamino, etc.] were prepared and formulated for use as vascular damaging agents in the treatment of a number of disease states

including cancer and rheumatoid arthritis. Thus, colchinol derivative II [R5 = OCO(CH2)2NHCOC2NH2] was prepared starting from N-acetylcolchinol, β-alanine Et ester hydrochloride, and N-(tert-butoxycarbonyl)glycine. Pharmaceutical compns. containing the prepared colchinol derivs. were also presented.

IT **281653-41-6P 281653-42-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of colchinol derivs. for use as vascular damaging agents for treatment of diseases such as cancer and rheumatoid arthritis)

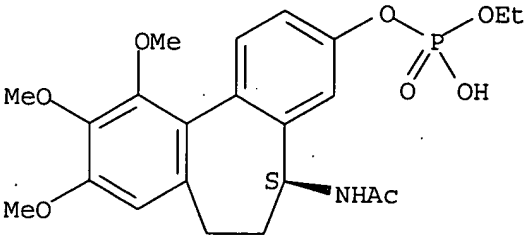
RN 281653-41-6 HCAPLUS
CN Phosphoric acid, mono[(5S)-5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-5H-dibenzo[a,c]cyclohepten-3-yl] monomethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281653-42-7 HCAPLUS
CN Phosphoric acid, mono[(5S)-5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-5H-dibenzo[a,c]cyclohepten-3-yl] monoethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

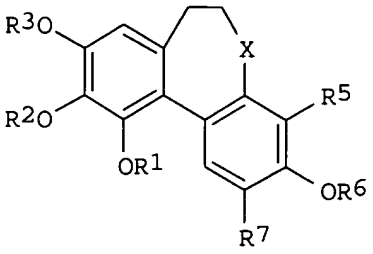
L15 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:64693 HCAPLUS
DOCUMENT NUMBER: 130:125254
TITLE: Preparation and formulation of colchinol derivs. useful for treatment of diseases involving angiogenesis
INVENTOR(S): Dougherty, Graeme
PATENT ASSIGNEE(S): Angiogene Pharmaceuticals Ltd., UK
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

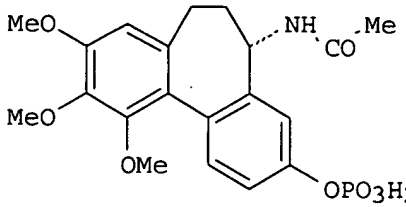
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9902166	A1	19990121	WO 1998-GB1977	19980706	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2292549	AA	19990121	CA 1998-2292549	19980706	<--
AU 9882311	A1	19990208	AU 1998-82311	19980706	<--
AU 741213	B2	20011129			
EP 1001785	A1	20000524	EP 1998-932374	19980706	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
BR 9810681	A	20000815	BR 1998-10681	19980706	<--
TR 9903149	T2	20000921	TR 1999-9903149	19980706	<--
NZ 501341	A	20010831	NZ 1998-501341	19980706	<--
JP 2001515516	T2	20010918	JP 1999-508313	19980706	<--
JP 3455549	B2	20031014			
RU 2232021	C2	20040710	RU 2000-102889	19980706	
ZA 9900106	A	19990707	ZA 1999-106	19990107	<--
MX 9911154	A	20000930	MX 1999-11154	19991202	<--
US 6423753	B1	20020723	US 2000-477805	20000105	<--
NO 2000000077	A	20000107	NO 2000-77	20000107	<--
PRIORITY APPLN. INFO.:			GB 1997-14249	A 19970708	
			WO 1998-GB1977	W 19980706	

OTHER SOURCE(S): MARPAT 130:125254

GI



I



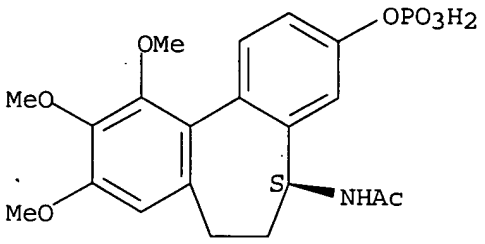
II

AB Colchinol derivs. I [R1, R2, R3, R6 = H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, alkanoyl, PO3H2; R5, R7 = H, alkyl, halogen, hydroxy, alkoxy, nitro, amino; X = CO, CS, CH2, CHR4, NR8R9; R4 = OH, alkoxy; R8 = H, alkyl, cycloalkyl, alkanoyl, thioalkanoyl, aryl, heteroaryl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, alkylsulfonyl, arylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl or arylaminosulfonyl; R9 = H, alkyl, cycloalkyl] were prepared and formulated for treatment of diseases involving angiogenesis. Thus, phosphate II was prepared via sequential O-phosphorylation of N-acetylcolchinol with (Me3CO)2PNEt2, P oxidation with MCPBA, and deesterification with TFA. The prepared compds were tested for

activity against turmor vasculature with the compds. having R6 = OPO3H2 as most preferred.

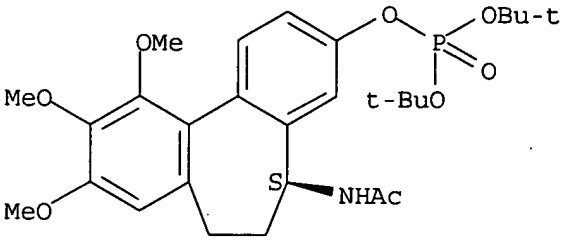
IT **219923-05-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and formulation of colchinol derivs. useful for treatment of diseases involving angiogenesis)
RN 219923-05-4 HCAPLUS
CN Acetamide, N-[(5S)-6,7-dihydro-9,10,11-trimethoxy-3-(phosphonooxy)-5H-dibenzo[a,c]cyclohepten-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **219923-15-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and formulation of colchinol derivs. useful for treatment of diseases involving angiogenesis)
RN 219923-15-6 HCAPLUS
CN Phosphoric acid, (5S)-5-(acetylamino)-6,7-dihydro-9,10,11-trimethoxy-5H-dibenzo[a,c]cyclohepten-3-yl bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	96.19	602.44
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-11.68	-11.68

STN INTERNATIONAL LOGOFF AT 10:32:49 ON 29 NOV 2005